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INTRODUCTION

The overall goal of this project was to investigate the physiological bases for chronic disequilibrium after combat-related TBI. Dizziness and imbalance are common symptoms in acute traumatic brain injury (TBI) and in some cases may persist chronically as part of the “post-concussive syndrome.” Little is known regarding the mechanisms underlying these symptoms. This project was based on the hypothesis that peripheral (inner ear) or central damage to vestibular pathways, particularly those based on otolith inputs, lead to imbalance and subjective disequilibrium after mild TBI (mTBI).

BODY

RESEARCH METHODS

Subjects

Three groups of subjects were enrolled in this study: 1) OEF/OIF/OND veterans with a history of mild TBI due to combat-related blast and/or blunt trauma who also reported ongoing chronic subjective disequilibrium, 2) OEF/OIF/OND veterans with a history of mTBI but no current vestibular symptoms, and 3) non-veterans with no history of TBI and no vestibular symptoms.

Nine veterans were enrolled into group 1, six veterans into group 2, and ten subjects into Group 3. Although recruitment challenges prevented us from reaching our original enrollment targets, we nonetheless have been able to demonstrate key physiological differences between these groups that provide new insights into the basis of these symptoms and that have potential application to the development and assessment of rehabilitation therapies.

Experimental Methods

There were two sets of data acquired in this study. First, we utilized an infrared motion tracking system (Vicon) in the Motion Study Laboratory of the Cleveland VAMC to record the kinematics of body motion during balance and locomotion tasks. Second, to assess the vestibular system, we studied the vestibulo-ocular reflexes by recording eye movements during linear and rotational motion of the head.

Static Balance

Infrared markers were placed on multiple locations of the body (Figure 1), including the head, neck, shoulders, waist, and lower extremities, for this and other balance and walking tasks. Instantaneous positions were recorded (100 Hz) by an array of infrared cameras surrounding the walkway. The analysis focused on a marker over the sacrum, whose motion represents motion of the pelvis and, for the upright position, approximates the motion of the body's center of mass.

Static balance tasks included standing on a firm surface (floor) and on a compliant surface (4” thick foam), both with eyes open and closed. We also tested subjects' range of voluntary weight shifting both from side-to-side and from left-to-right.

Dynamic Balance

Dynamic balance was assessed by recording postural responses to abrupt perturbations that were either in the forward or rightward direction. The perturbations were applied through a rope that was attached to a belt worn by the subject. The other end of the rope was connected to a computer-controlled linear actuator. Subjects were



FIGURE 1: Stick figure of one subject, reconstructed from recorded 3-D positions of infrared markers. Each white line connects two adjacent markers. Most of the analysis reported here was based on motion of the sacral marker, depicted in red.

tested with eyes both open and closed. For each condition, a block of ten trials was performed. The exact time of the perturbation was randomized so that it could not be predicted by the subject.

Locomotion

Gait was measured on a level walkway under three conditions: 1) walking on the floor with no obstacles, 2) walking onto and off a compliant surface (4" foam, approximately 6 m long), 3) stepping over a series of regularly spaced obstacles (12" high hurdles placed about 5 ft apart, depending on the individual subject's stride length). Each condition was repeated ten times, for a total of 30 walks.

Vestibulo-ocular Reflexes

On a computer controlled motion platform (Moog, Figure 2), we recorded eye movements in response to linear motion (translation) in the horizontal (interaural) and vertical directions. Head movement was recorded using a motion tracking system (Vicon) with infrared markers attached to the face. Eye movements were recorded with scleral coils or with video-oculography. The translational vestibulo-ocular reflex (tVOR) was tested with sinusoidal (2 Hz) and step motion profiles during fixation of a near target (15 cm). This tests the dynamic function of the otolith-mediated reflexes. The rotational VOR (rVOR) was tested with manually applied horizontal and vertical head impulses during visual fixation of a distant target (~ 2 m). Rotational head impulses assess the integrity of the reflexes driven by semicircular canal inputs.

Data Analysis

Kinematic Data for Balance and Gait

Vicon software reconstructs the position of each infrared target in three-dimensional space. Further analysis was conducted using custom programs written by the PI and engineers in Python and MATLAB. For static balance, the motion trajectories of the sacral marker for 5 seconds of recording were compared across conditions. The overall path length was determined by summing the sample-by-sample 2-D (forward-backward and side-to-side) line length over the 5 seconds. The instantaneous trunk angle was calculated from the sacral and cervical (C7) markers:

$$\theta_{trunk,roll} = \tan^{-1} \frac{x_{C7} - x_{sacrum}}{z_{C7} - z_{sacrum}} \quad \theta_{trunk,pitch} = \tan^{-1} \frac{y_{C7} - y_{sacrum}}{z_{C7} - z_{sacrum}}$$

where z is the vertical, x the lateral, and y the front-back marker position. For postural perturbations, the velocity and acceleration of the sacral marker were calculated. The perturbation onset was determined for each trial from the acceleration (see Figure 9), using a thresholding technique. Trials of each type were then aligned to the onset to calculate path length as a function of time.

For locomotion, we calculated mean forward gait speed for a 3 m segment within the center of each walk. Normalized path length (ratio of 2-D path length to forward path length) was calculated as a measure of the amount of side-to-side postural sway during walking under each condition.

Vestibulo-ocular Reflexes

For the tVOR, the head motion trajectory, as recorded by the infrared face markers, was used to determine the ideal eye movement that would keep the eye on the target. Eye movements evoked by linear motion depend on the distance of the object being viewed: near targets require much larger eye rotations than do

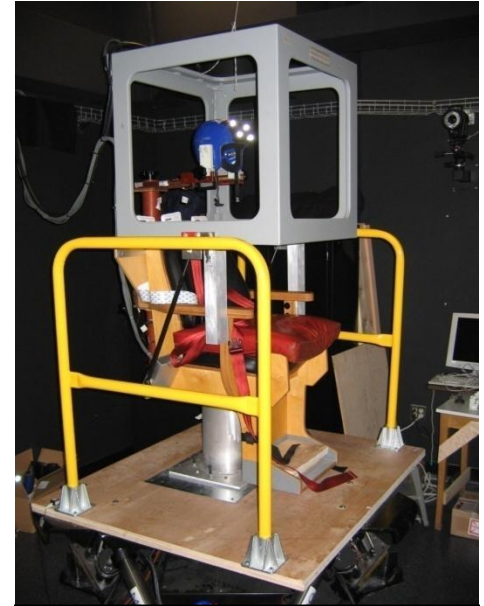


FIGURE 2: Moog motion platform for testing the vestibulo-ocular reflexes.

distant targets, based on geometrical considerations. Since the presumed goal of the VORs is to stabilize vision, responses are best quantified by how close the eye movement is to what would be required to keep gaze fixed on that particular target. The primary measure is a velocity gain g :

$$g = \frac{\omega_{actual}}{\omega_{ideal}}$$

where ω_{actual} is the actual recorded horizontal or vertical (depending on motion direction) angular eye velocity and ω_{ideal} is the ideal velocity that would stabilize gaze. A gain of unity indicates full stability and a gain of zero no response.

Statistical Tests

Unless otherwise noted below, we used multivariate repeated-measures ANOVA (function `aov` in R, www.cran.r-project.org) to determine the effects of both between-group (e.g., presence/absence of mTBI and disequilibrium) and within-subjects (e.g., eye closure, standing or walking surface, perturbation direction) on the outcome measures. Due to non-normality of the outcome measures, particularly in the mTBI group, logarithmic transformation of the outcome measure was used.

RESULTS

Summary of Research Findings

- mTBI veterans with disequilibrium have decreased static postural stability, particularly when standing with eyes closed and when standing on a compliant surface
- mTBI veterans with disequilibrium have decreased dynamic postural stability (increased body sway) when perturbed in either the forward or lateral direction
- mTBI veterans with disequilibrium have increased variability of postural responses to perturbation, as well as less well organized responses that include higher frequency oscillations
- mTBI veterans with disequilibrium demonstrate decreased gait speeds when walking on both firm and compliant surfaces
- mTBI veterans with disequilibrium have increased lateral sway (longer path lengths) during walking.
- mTBI veterans have a trend toward decreased tVOR gains, especially for horizontal translations. The group difference did not reach statistical significance due to overlap, but 4/9 mTBI subjects with disequilibrium had horizontal tVOR gains that fell below those of all non-TBI subjects and the relationship of horizontal to vertical tVOR gain was significantly different.

Static Postural Stability

Figure 3 depicts the postural stability of two subjects (one without TBI and one with mTBI and disequilibrium). The TBI subject has a greater range of sway, especially without vision, and a greater amount of upper body tilt. Both of these cause shifts of the body's center-of-mass away from the feet and may lead to an increased risk of falling, particularly when proprioceptive and visual cues are unavailable or less reliable.

Postural stability of each group is compared in Figure 4 in the form of data ellipses for aggregate data from all subjects. The findings are consistent with the examples of Figure 3 and also show a clear difference in postural sway between the two mTBI groups: stability overall is worse in mTBI veterans who themselves report chronic dizziness and imbalance. This makes it more likely that these findings represent a physiologic correlate to those symptoms.

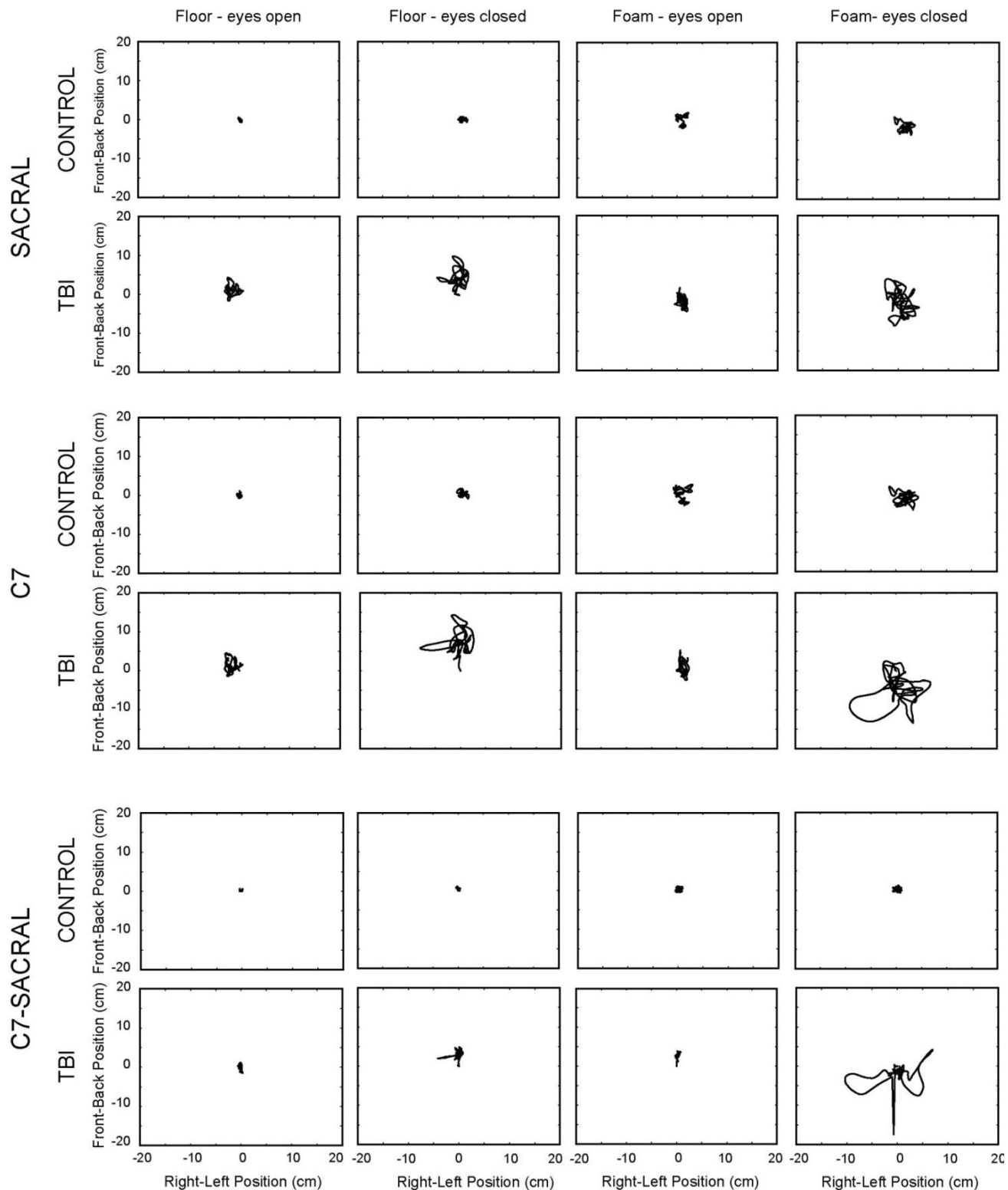


FIGURE 3: Two-dimensional postural sway during 5 seconds of quiet standing with eyes open (EO) or closed (EC) on a firm (floor) or compliant (4" foam) surface for a non-TBI subject (CONTROL) and a TBI subject with disequilibrium. The top two rows show the motion of the sacral marker (pelvis) and the middle two rows the motion of the C7 marker, both relative to the floor. The last two rows show the motion of C7 relative to the sacrum. The increased range of motion in the TBI subject indicates a greater amount of tilt of the trunk relative to the lower body.

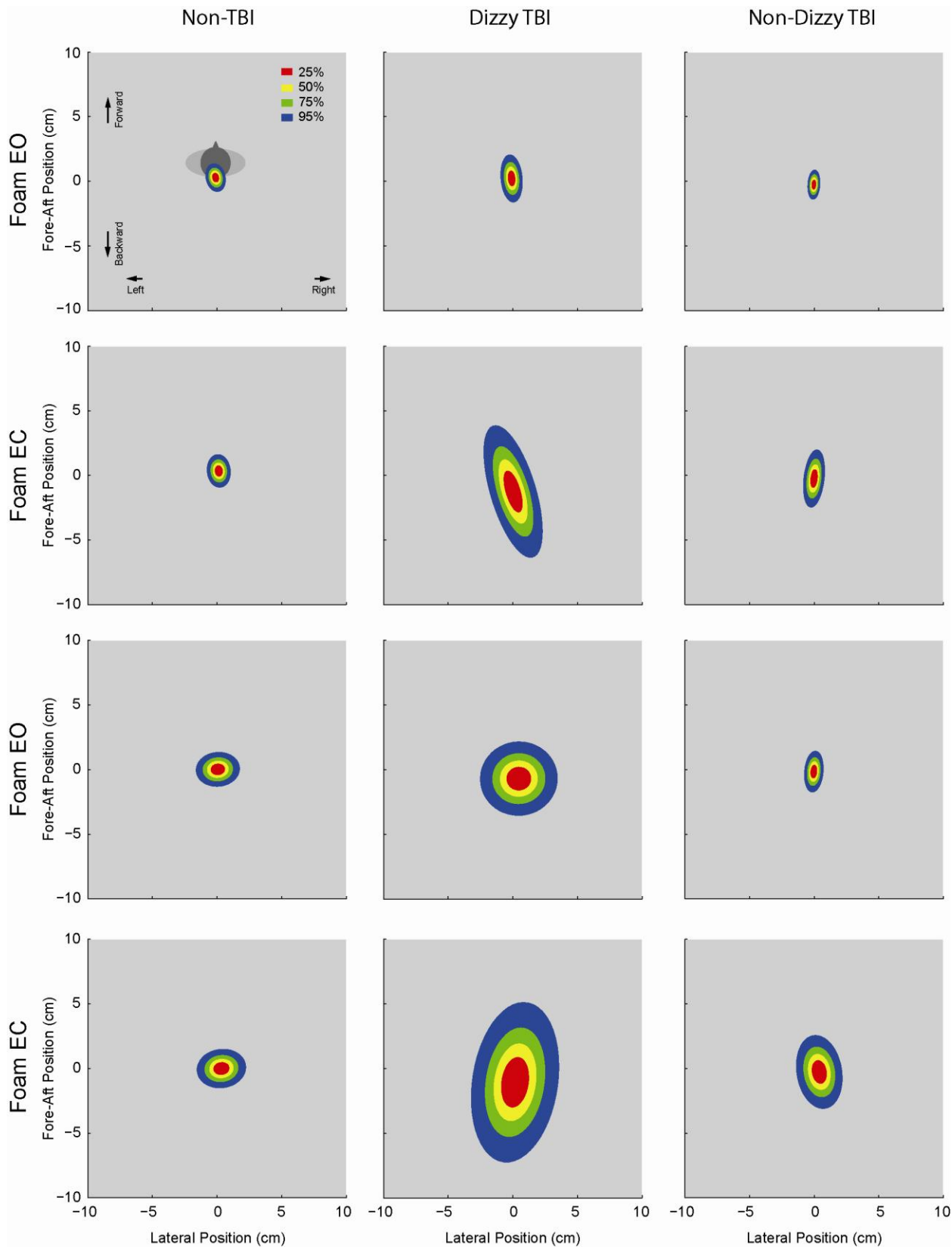


FIGURE 4: Two-dimensional postural sway during 5 seconds of quiet standing with eyes open (EO) or closed (EC) on a firm (floor) or compliant (4" foam) surface. The data ellipses encompass the first three quartiles (25%, 50%, 75%) and 95% of aggregate data for all subjects in each group. The TBI subjects reporting disequilibrium (center column) have the greatest amount of sway.

Postural sway was quantified by the total path length of the sacral marker during 5 seconds of recording. The effects of mTBI and symptomatic disequilibrium were assessed using a repeated-measures ANOVA in R, based on the following model:

$$\log(\text{Length}) \sim \text{mTBI} * \text{Disequilibrium} * \text{EyeClosure} * \text{StandingSurface}$$

with mTBI (yes vs. no) and disequilibrium (yes vs. no) as between-groups factors and eye closure (open vs. closed) and standing surface (floor vs foam) as within-subjects factors. The effects of all factors were significant: mTBI ($p < 0.0005$), disequilibrium ($p < 0.003$), surface ($p < 10^{-5}$), and eye closure ($p < 10^{-8}$).

mTBI veterans also had increased relative sway of the upper body, as measured by the trunk angle, particularly when standing with eyes closed on foam (Figure 5).

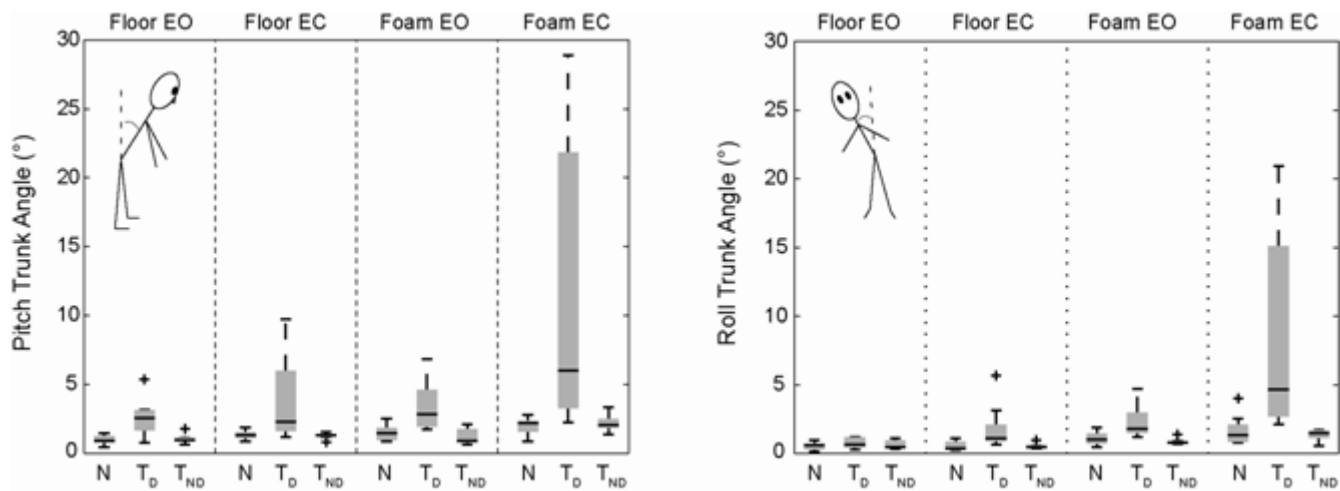


FIGURE 5: Trunk angle range (difference of maximum and minimum angles) determined from the 3-D positions of the sacral and C7 infrared markers for each group (N=normal, T_D=TBI with disequilibrium, T_{ND}=TBI without disequilibrium). The TBI subjects with disequilibrium had much more sway of the upper body when standing on foam with eyes closed. The trunk angles of subjects without disequilibrium were similar to those without TBI under all conditions.

Dynamic Postural Stability

Responses to forward and rightward postural perturbations are shown in Figure 6 for an mTBI veteran with disequilibrium and a non-TBI subject. In the mTBI veteran, postural corrections are less accurate, slower, and more variable. Similar to static balance, we calculated the sway path length from perturbation onset, in this case at 0.5 second intervals up to 2.5 seconds from the pull. Results are summarized by the box plot of Figure 7.

As for static posture, we used a multivariate ANOVA to determine the effects of mTBI and disequilibrium on responses to perturbations:

$$\log(\text{Length}) \sim \text{mTBI} * \text{Disequilibrium} * \text{EyeClosure} * \text{PullDirection}$$

The interaction term *Disequilibrium*EyeClosure* had a statistically significant effect ($p < 0.002$). The effect of eye closure for veterans with disequilibrium can also be seen in the scatter plot of Figure 8.

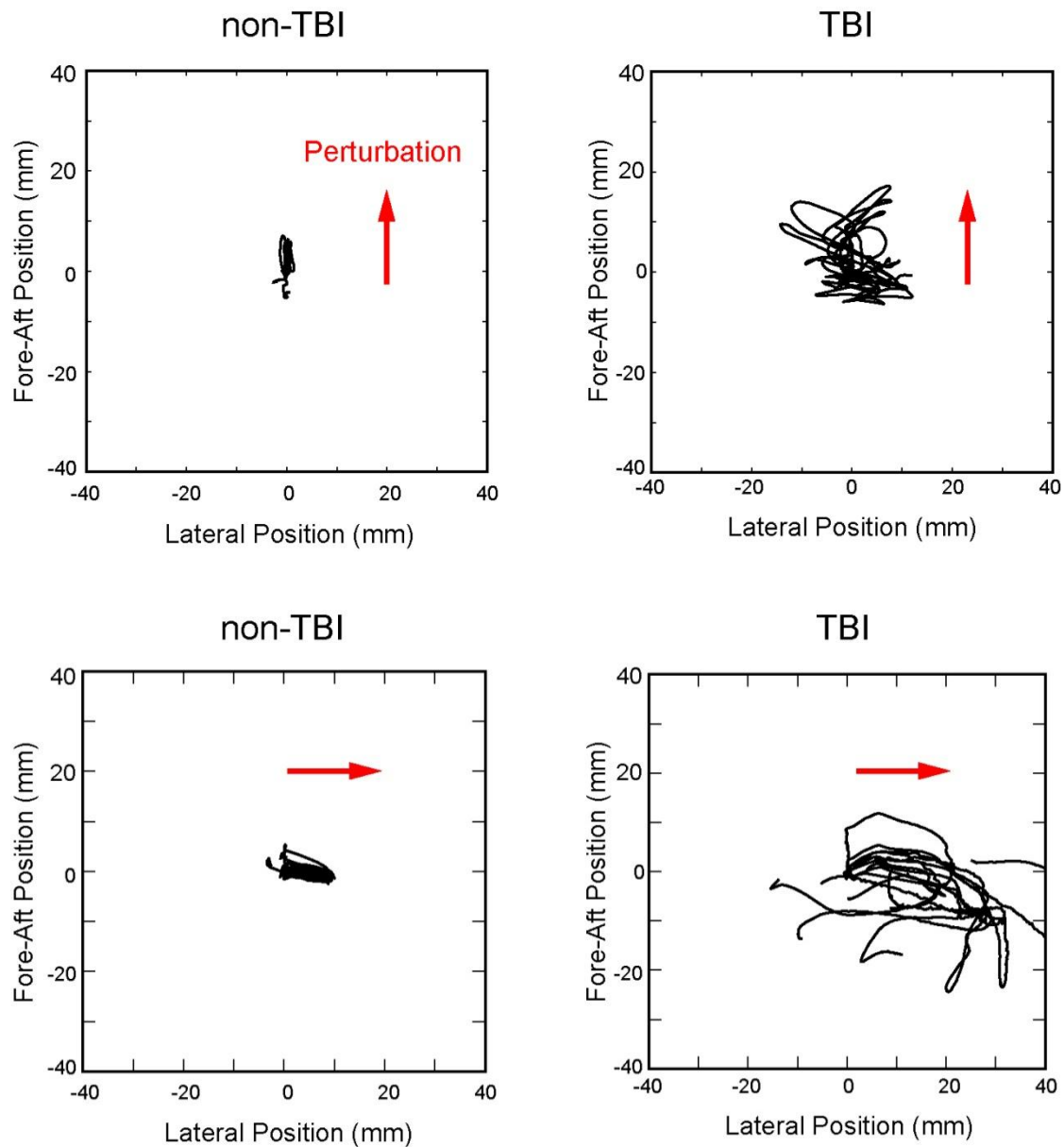


FIGURE 6: 2-D path of the sacral marker (from the starting position=(0,0)) for the first 2.5 seconds after the onset of the perturbation (as determined by the marker acceleration profile). Responses from similar trials are superimposed. Note that the non-TBI subject has a much smaller range of motion and by the end of the interval is back very close to the initial position. In contrast, the mTBI veteran with disequilibrium has greater postural displacement and more variable responses. For most trials, the ending position is as much as several centimeters away from the initial location.

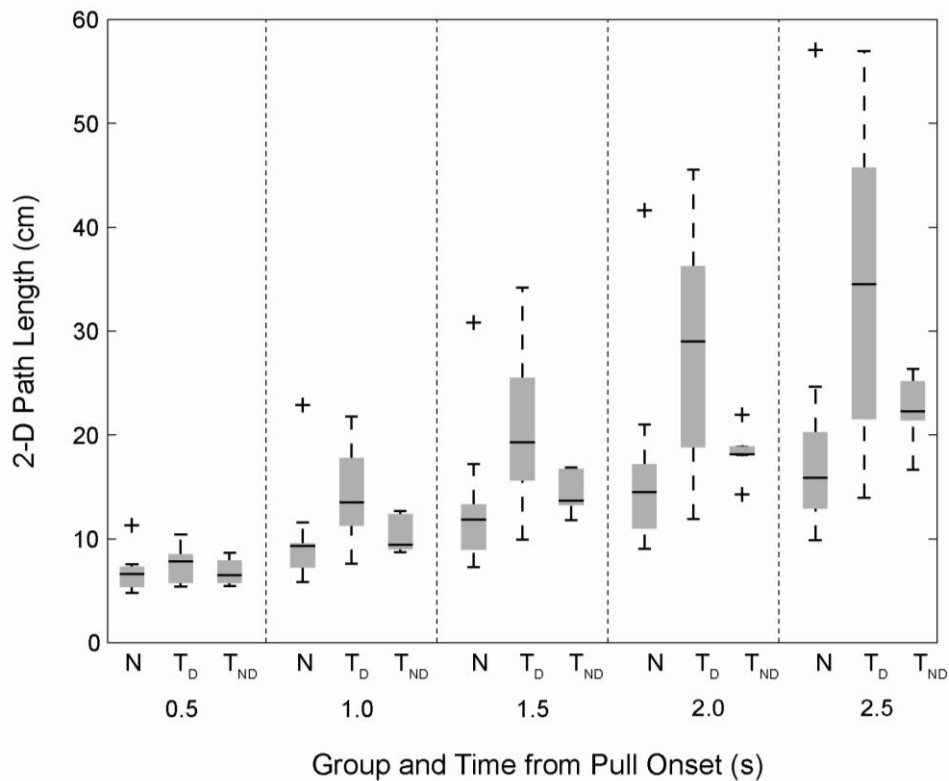


FIGURE 7: Forward perturbation with eyes closed. Boxplot of 2-D sway path length (pelvis) for each group at 5 time points from the onset of the perturbation (N=normal, T_D=TBI with disequilibrium, T_{ND}=TBI without disequilibrium).

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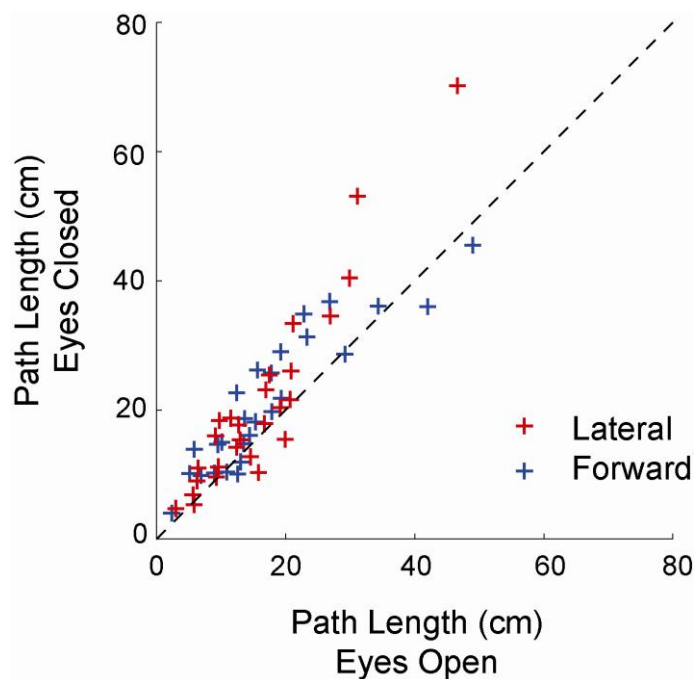


FIGURE 8: Sway path length for mTBI subjects with disequilibrium, comparing eyes-open to eyes-closed condition for both pull directions

As can be seen in the position plots of Figure 6, mTBI veterans with disequilibrium not only had greater postural sway when perturbed but also had more disorganized and variable responses. This can be seen clearly by comparing the velocity and acceleration profiles of the non-TBI subject and the mTBI disequilibrium subject (Figure 9). We quantified the trial-to-trial variability by calculating the instantaneous variance as a function of time and summing that over the full 2.5 seconds. The results are shown in Figure 10. Although there were outliers in each group, overall the mTBI disequilibrium group had a higher variance in each condition. This is a key finding because it may represent a physiological signature of this symptom and could also be a marker of the presence of mTBI and its resolution, as veterans with an mTBI history who no longer had dizziness or imbalance did not show this motor disturbance.

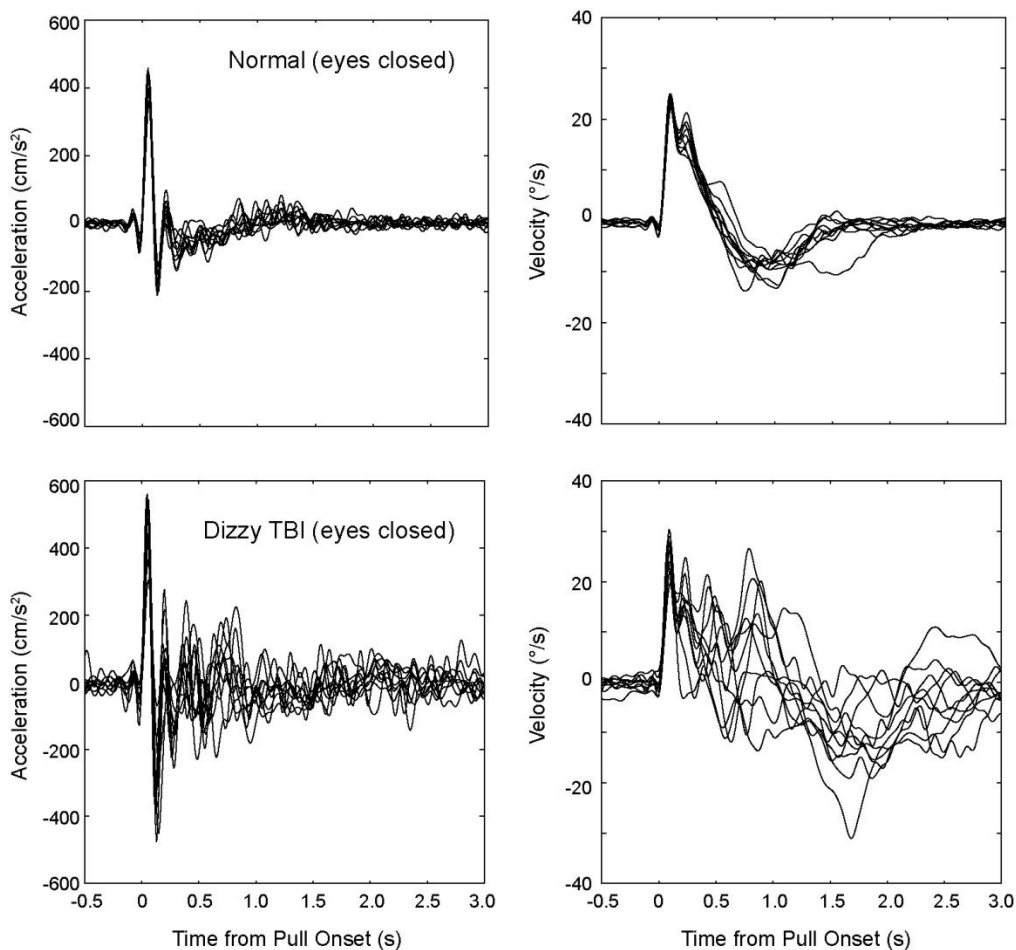


FIGURE 9: Forward acceleration and velocity of the sacral marker in response to forward perturbations. Trials are aligned to pull onset ($t=0$).

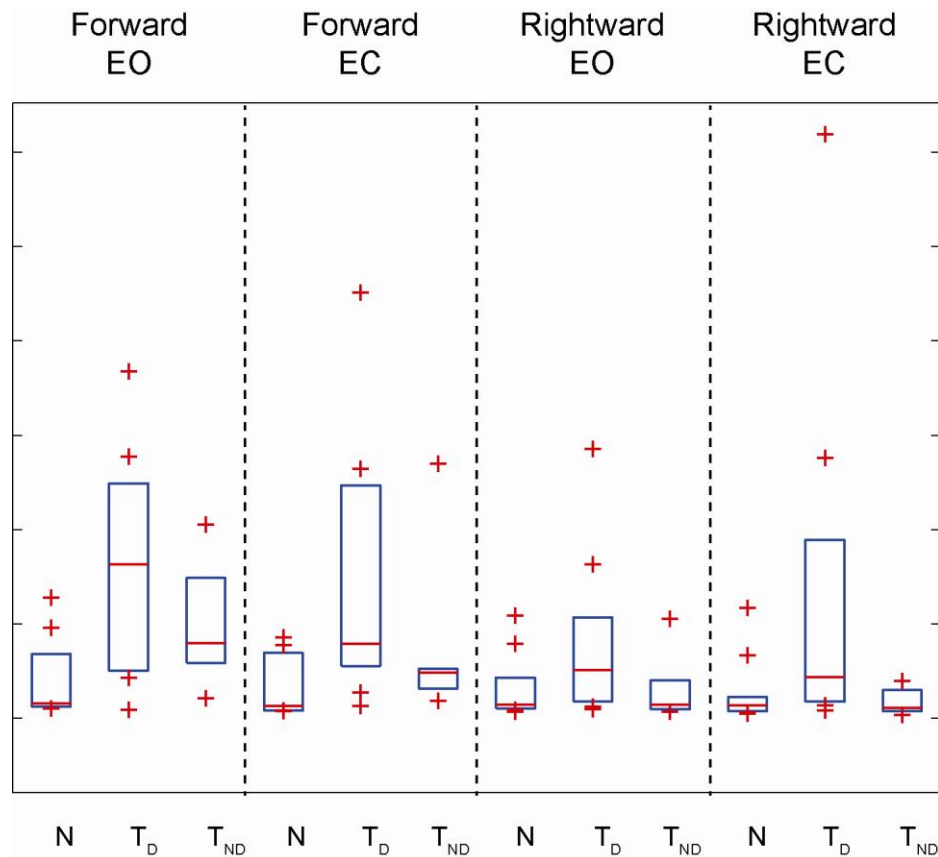


FIGURE 10: Trial-to-trial variance of forward perturbations (summed for 2.5 s after pull onset).

Gait Speed and Path Length

From reconstructed kinematic data, we calculated mean gait speed (sacral marker) for each walk and then the mean of all trials for a given condition in each subject. The results are presented in the box plot of Figure 11. There was a trend toward slower walking in the mTBI disequilibrium group, but this was not statistically significant ($p < 0.18$). Gait path length, however, was longer for the subjects with disequilibrium (Figure 12, $p < 0.01$). Because path lengths were normalized to the distance walked in the forward direction, longer path lengths suggest increased postural sway during walking, consistent with the findings for static postural stability (Figure 4). Additional analysis of locomotion will include an assessment of gait kinematics.

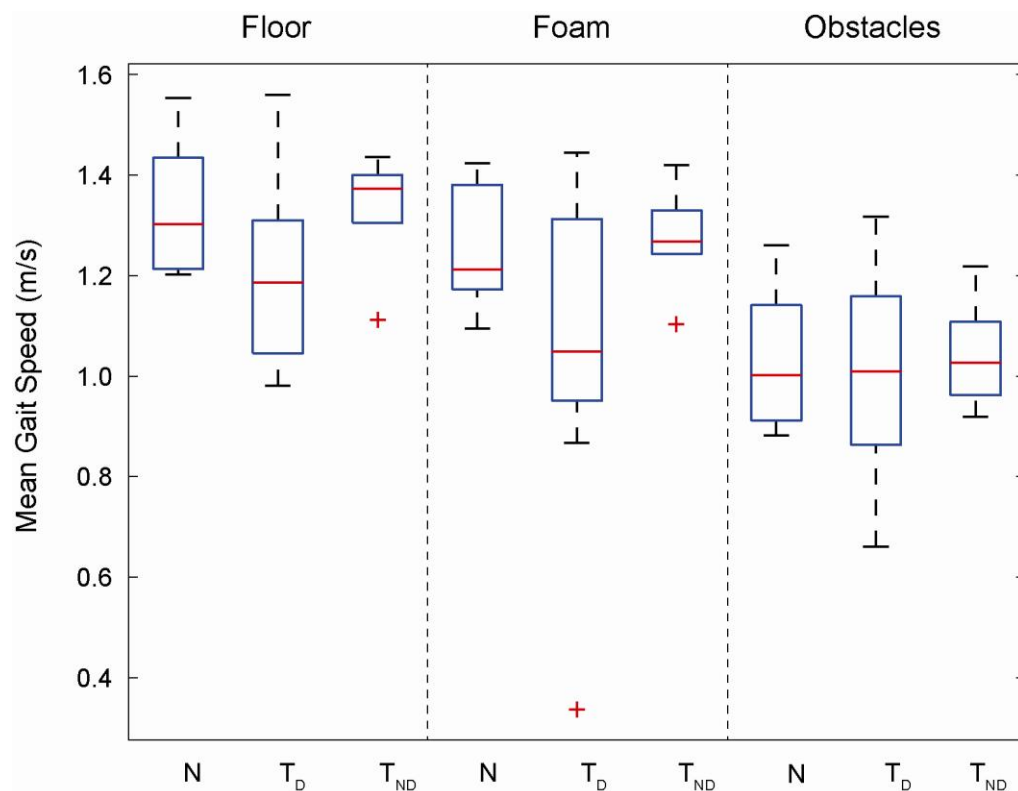


FIGURE 11: Box plot of mean gait speeds for each subject group under all three conditions: 1) level walking on the floor, 2) walking on a compliant surface (4" foam), 3) walking while stepping over obstacles.

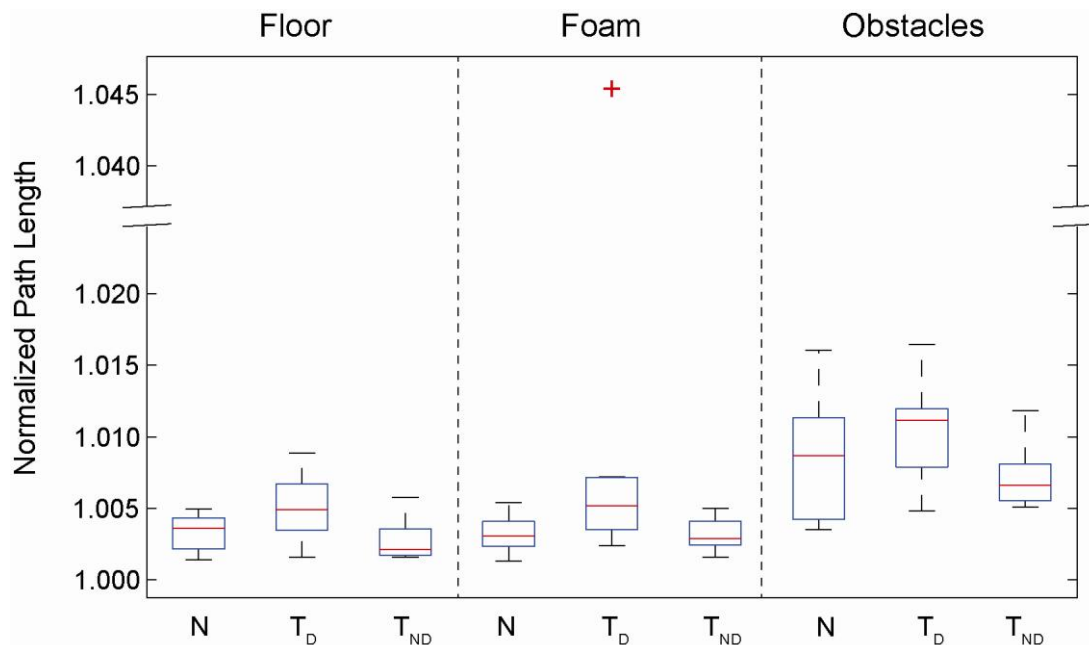


FIGURE 12: 2-D path length (average of all similar trials for each subject) for walking trials under each of the three conditions. Lengths were normalized to the forward path length

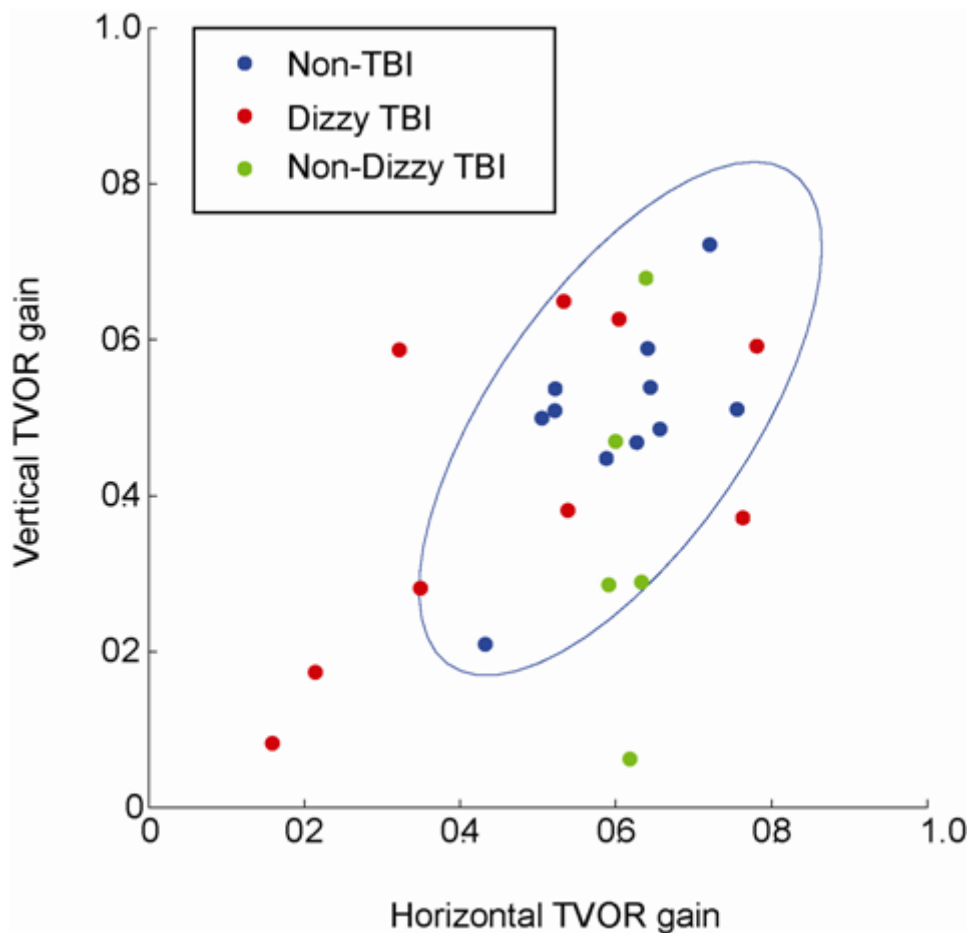


FIGURE 13: Gains for the translational vestibulo-ocular reflex for 2 Hz horizontal and vertical sinusoidal motion. The gain is calculated as the ratio of the amplitude of the recorded eye velocity to the amplitude of the ideal eye velocity that would keep visual fixation steady on the target (distance 15 cm from the eyes). The blue circle shows the 95% data ellipse for 12 non-TBI subjects.

tVOR Gains

Figure 13 shows tVOR gains for steady-state 2 Hz translation in the horizontal (interaural) and vertical directions. Although there was overlap between groups, tVOR gains appeared to be scattered more widely for the mTBI subjects. Gain values for 4 of the mTBI veterans with disequilibrium and 1 without disequilibrium fell out of the 95% data ellipse for normal subjects (blue ellipse in Figure 13). The differences appear most notable for horizontal translation: four subjects with disequilibrium had horizontal tVOR gains that were lower than any subject without disequilibrium (with or without TBI). A multivariate ANOVA based on the following model:

$$\text{Gain} \sim \text{TBI} * \text{Disequilibrium} * \text{MotionDirection}$$

found significant effects of motion direction ($p < 0.002$) and of the interaction between disequilibrium and motion direction ($p < 0.05$). The latter finding suggests a different relationship between the motion direction and gain for the disequilibrium group: lower horizontal relative to vertical tVOR gains for these subjects. Following this up with an ANOVA of the following model:

$$\text{Horizontal Gain} \sim \text{Vertical Gain} * \text{TBI} * \text{Disequilibrium}$$

demonstrated a significant effect of both vertical gain ($p < 0.01$, gains for the two motion directions are correlated) and for disequilibrium ($p < 0.03$, this symptom had an independent effect on the horizontal tVOR gain). This finding suggests a relative impairment of the otolith-driven dynamic reflexes that depend on inputs from the utricle, and it supports our hypothesis that impaired otolith reflexes contribute to dizziness and imbalance after mTBI.

KEY RESEARCH ACCOMPLISHMENTS

- We have studied static and dynamic balance, gait, and vestibular function in detail in veterans with combat-related mTBI and have found a series of physiological correlates of chronic subjective disequilibrium, even months to years after an injury. This is an important finding, because the persistence of physically-based symptoms after these seemingly mild injuries has been questioned in some circles. It is difficult to imagine that all of these physiological abnormalities could be attributed solely to psychological causes.
- We have found that these physiological markers are specific to those mTBI veterans who still have symptoms and are not present in those with mTBI who are no longer dizzy. This suggests that one or more of these measures may be an effective tool for the detection of mTBI/concussion and for following it to its recovery. They might also be useful for the stratification of risk of activity after mTBI in a way that could contribute to decisions regarding return to combat or other activities.
- We have found that mTBI veterans with disequilibrium not only have impaired static and dynamic balance but also have disorganized, abnormal motor responses to perturbations. Although not fully conclusive, these findings suggest that the balance abnormalities are not simply due to a sensory impairment (e.g., peripheral vestibular) but involve at least in part a motor control deficit.
- Veterans with mTBI and disequilibrium had relatively lower responses to horizontal translation (linear motion) than mTBI and non-TBI subjects without disequilibrium.

REPORTABLE OUTCOMES

- Findings of this study were reported at the following meetings:
 - NATO Human Factors in Medicine Panel HFM-207: A Survey of Blast Injury across the Full Landscape of Military Science, Halifax, NS, Canada, October 2011. (conference proceeding paper attached in Appendix)
 - North American Brain Injury Society (NABIS) Tenth Annual Conference on Brain Injury, Miami, FL, September 2011 (abstract attached in Appendix).
- Manuscripts based on the experimental findings presented in this report are being finalized for submission and will be submitted to the USAMRMC upon acceptance.
- Grant applications based on these findings are in preparation but not yet submitted

CONCLUSION

In this study we have identified disturbances of static and dynamic posture, gait, and vestibular function that are specific to chronic disequilibrium after mTBI due to combat-related head trauma. There are several key implications of these results. First, it is possible to demonstrate a measurable physiological correlate to an otherwise vague subjective somatic symptom that is difficult to discern in a basic examination. This suggests that although most individuals with such injuries recover, there may still be subtle neurological deficits that persist long-term and that are not simply due to psychological causes. Second, such physiological

measures could provide a more robust signature of an acute injury and a measure that can be followed over time in the context of spontaneous recovery and directed rehabilitation. Third, the ability to quantify these deficits precisely may provide a tool that can estimate the risk of repeat injury and can aid decisions regarding return to duty or other activity.

Suggested further study would include a similar assessment closer to the time of acute injury and a tracking of these measures over time both as a means to document and understand the normal recovery process and response to treatment and to look for markers that may predict incomplete recovery and persistence of symptoms.

BIBLIOGRAPHY

1. Walker MF, Liao K, Pan T, Roenigk K, Daly J. Postural Instability in Blast-Exposed Veterans. In: RTO-MP-HFM-207- A Survey of Blast Injury across the Full Spectrum of Military Science. Paper 36, 2011. <https://www.cso.nato.int/Pubs/rdp.asp?RDP=RTO-MP-HFM-207>
2. Walker M, Pan T, Liao K. Dynamic Postural Instability in OEF/OIF Veterans with Mild TBI and Disequilibrium (Abstract). North American Brain Injury Society's Tenth Annual Conference on Brain Injury. *J Head Trauma Rehabil* 27(5):E34, 2012.

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ABSTRACT

Dizziness and imbalance are common in post-concussive syndrome after blunt head trauma and have also been reported in service members with mild traumatic brain injury (mTBI) due to explosions. Quantitative assessments are limited, particularly in the military population, and the mechanism of balance impairment is poorly understood. The purpose of this study was to measure postural stability in veterans with persistent disequilibrium after combat-related mTBI.

Seven veterans deployed to Operation Enduring Freedom (OEF) and/or Operation Iraqi Freedom (OIF) with a history of mTBI and persistent disequilibrium and five healthy volunteers without a history of blast exposure were studied. A motion tracking system was used to record leg and trunk kinematics during quiet standing on a hard floor and on a foam surface, both with eyes open and closed. Postural stability was quantified by calculating body sway (root-mean-square (RMS) displacement in two dimensions) at the waist (sacral marker).

Under all conditions, the RMS displacement of the sacral marker was 2.3-4 times as large for the mTBI group. The group difference ($p < 0.04$) and eyes open vs closed ($p < 0.003$) were both significant. The greatest balance impairment was in mTBI veterans standing on foam with eyes closed. Postural stability in the mTBI group while standing on the hard floor with eyes open was similar to that in healthy subjects standing on foam with eyes closed.

Our findings confirm that disequilibrium in veterans with a history of mTBI is associated with decreased postural stability, particularly under more challenging conditions.

1.0 INTRODUCTION

It has been estimated that 5 to 20% of troops deployed to Iraq and Afghanistan have experienced a mild traumatic brain injury (mTBI) due to blast or blunt trauma (reviewed in Carlson et al. 2011). Although most of these are expected to recover without functional neurological sequelae, persistent symptoms after injury, similar to the post-concussive syndrome reported after civilian mTBI, are not uncommon. Dizziness and disequilibrium are among the symptoms that are commonly reported, and in many cases these symptoms may persist and become chronic. For example, one study showed that 12% of service members with blast-related amputations had chronic dizziness (Scherer et al. 2007), and in another study, 15% of 258 blast-exposed service members reported dizziness (Cave et al. 2007).

Prior studies, mostly in civilians, have shown that balance and posture may be impaired after mTBI, as evidenced, for example, by lower scores on clinical posturography (Basta et al. 2005; Kaufman et al. 2006). Impaired balance correlates with the subjective symptom of disequilibrium, measured by the Dizziness Handicap Inventory (Kaufman et al. 2006).

Fewer data are available regarding balance after mTBI that occurs in the military setting, although abnormal clinical posturography has been reported in veterans with mTBI (Akin and Murnane 2011). The goal of the present study is to quantify postural stability, using infrared-based measurements of body kinematics, in veterans with chronic disequilibrium after mTBI, and to compare them to a group of non-deployed subjects with no history of TBI or imbalance.

2.0 METHODS

2.1 Subjects

We studied seven OEF/OIF veterans with a history of combat-related mTBI who reported persistent disequilibrium and imbalance, and five non-veterans with no history of TBI nor vestibular or neurological problems. All subjects gave written informed consent under a protocol that was approved by the Institutional Review Boards of the Louis Stokes Cleveland Department of Veterans Affairs Medical Center (LSCDVAMC) and of the University Hospitals of Cleveland Case Medical Center, as well as by the Human Research Protection Office of the United States Department of Defense, in accordance with the Declaration of Helsinki.

2.2 Balance Testing and Data Recording

Balance was tested during quiet standing under four conditions of increasing difficulty: 1) standing on a hard floor with eyes open, 2) standing on the floor with eyes closed, 3) standing on a compliant foam surface (approximately 10 cm thick) with eyes open, and 4) standing on the foam surface with eyes closed.

An infrared motion tracking system (Vicon) was used to record body kinematics during standing. For the purpose of this study, we focused our analysis on the motion of the pelvis (as measured by an infrared marker placed over the sacrum). Marker data were sampled at 100 Hz and saved for subsequent analysis.

2.3 Data Analysis

Three-dimensional marker positions were reconstructed by the Vicon software. Subsequent analysis was performed using custom programs, written by the authors in Python and MATLAB™. For each of the four conditions, we quantified postural stability by calculating the root-mean-square (RMS) of the two-dimensional (in the horizontal plane) displacement from the start position, over the first five seconds of recording. We compared results in the two groups using a repeated-measures ANOVA (ezANOVA package) in R (www.cran.r-project.org).

3.0 RESULTS

3.1 Example Responses

Representative sway data are depicted in Figure 1 for one control subject and one mTBI subject for two test conditions: standing on the floor with eyes open and standing on foam with eyes closed. Each plot traces the two-dimensional path of the sacral marker during the first three seconds of recording. The x-axis shows the instantaneous position in the coronal plane (left-to-right) and the y-axis the position in the sagittal plane (forward-to-backward).

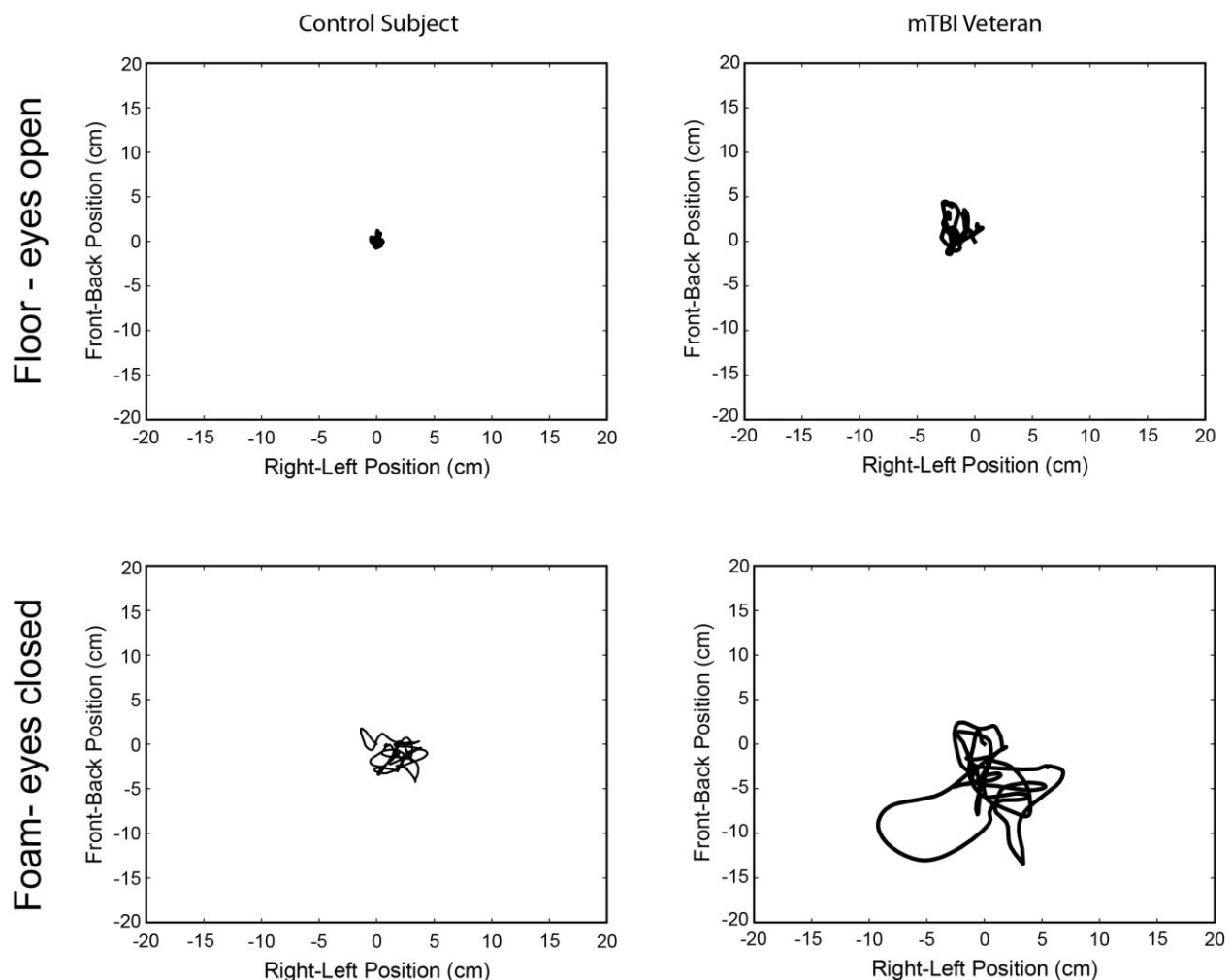


Figure 1: Example sway paths in one control subject and one mTBI veteran under two conditions: standing on the floor with eyes open (the easiest condition) and standing on foam with eyes closed (the most difficult condition). As expected, both subjects demonstrated more sway of the pelvis in the second condition.

3.2 Summary Data

Summary data for all subjects are shown in Figure 2. Although instability varied among individual subjects, veterans with mTBI had larger RMS displacements under all conditions than did normal subjects. The difference in postural stability between the two groups was most notable when the eyes were closed. The median displacement was 3.7 times greater for mTBI veterans than control subjects when standing on

the floor with eyes closed, and 2.6 times greater when standing on foam with eyes closed. Even standing on the floor with eyes open (the easiest condition), however, the veterans had larger postural sway. The median displacement for mTBI veterans standing on the floor with eyes open was similar to that of control subjects when standing on foam with eyes closed.

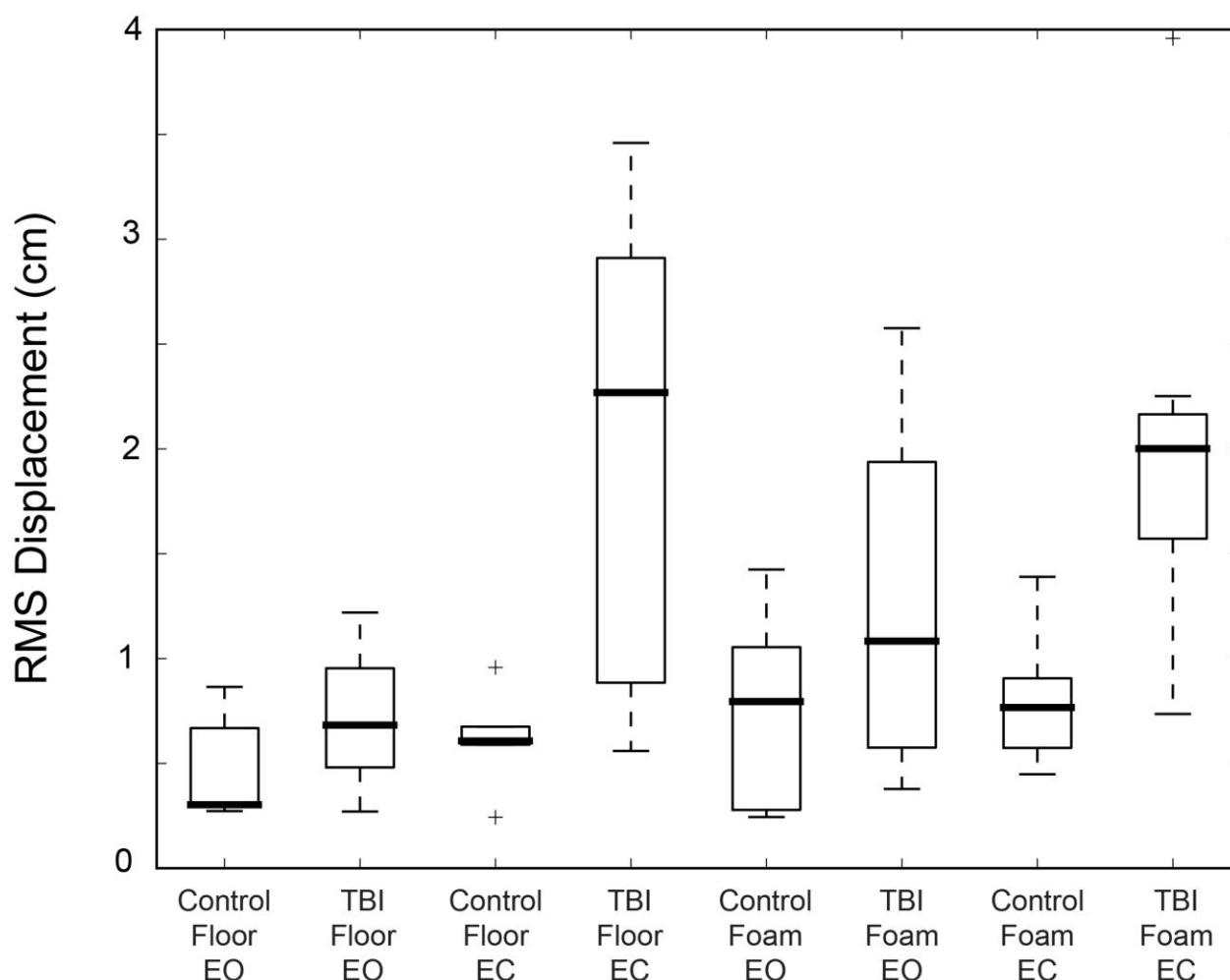


Figure 2: Box and whisker plot of RMS displacements measured at the sacral marker for control subjects and veterans with mTBI, while standing on the floor and on foam with eyes open (EO) and closed (EC). The thick lines show the median value for each group, the box the 25% to 75% percentiles, and the whiskers show the full range of data, with the exception of outliers (indicated with a '+').

4.0 DISCUSSION

Our results show that OEF/OIF veterans who have experienced combat-related mTBI and report chronic dizziness have measurable balance deficits on both firm (floor) and compliant (foam) surfaces. Their balance is most impaired when vision is removed (during eye closure) but even in the simplest condition, standing on the floor with eyes open, their posture is less stable.

The mechanism of impaired balance after mTBI remains uncertain and may be multifactorial. The fact that balance is much worse with eyes closed than open is consistent with a deficit in the central or peripheral vestibular system, although recent evidence, primarily from clinical testing, suggests that peripheral and

central vestibular deficits may be present after mTBI (Akin and Murnane 2011; Scherer et al. 2011b; Scherer et al. 2011a). Postural deficits that substantially worsen in the dark would be consistent with a vestibulospinal disorder, but further study is needed to provide direct evidence to support this idea.

There are several limitations to this study. First, the number of subjects is small and the mTBI group is heterogeneous. Many variables are likely to contribute to the severity of injury in a particular individual, such as the nature, size, and proximity of the blast, and the presence or absence of concomitant blunt head trauma. Due to the context of these injuries, detailed documentation of the exposures and injuries is not available, and thus injury differences cannot be taken into account in the interpretations of the results.

A second limitation is that these veterans were not studied acutely but many months after their injuries, during which time they may have experienced some neurological recovery. Thus, it may be that our measurements underestimate the amount of imbalance that is present acutely after injury. Nonetheless, our findings are important, because they show that these injuries can cause chronic balance deficits that do not spontaneously recover.

In summary, we have found that some combat veterans with a history of mTBI have impaired balance, especially with eyes closed. Even with eyes open their balance is worse than that of controls. Postural sway of mTBI veterans was similar when standing on the floor with eyes open to the sway of control subjects standing on foam with eyes closed. These findings are significant, because veterans with disequilibrium do not typically exhibit balance impairment during routine clinical examination. Our results suggest, however, that in a physically challenging environment, they may be at risk for falls and further injury.

5.0 REFERENCES

- Akin FW and Murnane OD.** Head injury and blast exposure: vestibular consequences *Otolaryngol Clin North Am* 44: 2: 323-34, viii, 2011.
- Basta D, Todt I, Scherer H, Clarke A and Ernst A.** Postural control in otolith disorders. 24: 2: 268-279, 2005.
- Carlson KF, Kehle SM, Meis LA, Greer N, Macdonald R, Rutks I, Sayer NA, Dobscha SK and Wilt TJ.** Prevalence, assessment, and treatment of mild traumatic brain injury and posttraumatic stress disorder: a systematic review of the evidence *J Head Trauma Rehabil* 26: 2: 103-115, 2011.
- Cave KM, Cornish EM and Chandler DW.** Blast injury of the ear: clinical update from the global war on terror. *Mil Med* 172: 7: 726-730, 2007.
- Kaufman KR, Brey RH, Chou LS, Rabatin A, Brown AW and Basford JR.** Comparison of subjective and objective measurements of balance disorders following traumatic brain injury. *Med Eng Phys* 28: 3: 234-239, 2006.
- Scherer M, Burrows H, Pinto R and Somrack E.** Characterizing self-reported dizziness and otovestibular impairment among blast-injured traumatic amputees: a pilot study. *Mil Med* 172: 7: 731-737, 2007.
- Scherer MR, Burrows H, Pinto R, Littlefield P, French LM, Tarbett AK and Schubert MC.** Evidence of central and peripheral vestibular pathology in blast-related traumatic brain injury *Otol Neurotol* 32: 4: 571-580, 2011a.
- Scherer MR, Shelhamer MJ and Schubert MC.** Characterizing high-velocity angular vestibulo-ocular reflex function in service members post-blast exposure *Exp Brain Res* 208: 3: 399-410, 2011b.



effects of demographic, etiology, discharge disability, and socio-environmental factors.

Method/Approach

Participants were adults (18 years or older) who sustained a TBI July, 2001 to December, 2009 and were alive 1-year post-injury. Identification was through the TBI Model Systems National Database, a network of institutions providing specialty care in the United States. Mortality was identified using the Social Security Death Index. Person-year logistic regression analysis was used to identify the odds of mortality. There were 5,806 1-year survivors with 19,683 person-years and 362 deaths.

Results/Effects

Among 1-year survivors, fall and violent etiologies, male gender, white race, and higher age were significantly associated with greater odds of mortality. Persons not independent in feeding at rehabilitation discharge were at increased odds of mortality; however, unconsciousness and ability to walk at rehabilitation discharge were not predictive of mortality. Among the socio-environmental predictors, higher personal income was protective of mortality. Pre-injury education and marital status were not significantly related with mortality.

Conclusions/Limitations

Socio-environmental factors, specifically income, at TBI onset appear to be highly related to post-TBI mortality, even after accounting for demographic status and multiple other factors. Future studies are needed that provide updated socio-environmental information (not just that available at rehabilitation) to assess the effect of change in socio-environmental status. Additionally, behavioral variables should be investigated as they are potentially modifiable factors.

0078

Chiropractic Sacro Occipital Technique (SOT) and Cranial Treatment Model for Traumatic Brain Injury Along with Monitoring and Supplementing for Neurotransmitter Balance: A Case Report.

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Introduction/Rationale

The purpose of this paper is to present a novel treatment model incorporating laboratory testing to evaluate neurotransmitter balance and chiropractic cranial care for the treatment of a patient with traumatic brain injury (TBI). A 33-year-old female presented at this office for care secondary to an attack that included strangulation and repeated facial trauma. Her main symptom was chronic debilitating headaches unresponsive to rest, medication, or other interventions. Prior to being seen at this office she was under the care of a neurologist and taking medications, which caused her extreme side-effects, yet did not relieve her headaches.

Method/Approach

She has been under care for three years, which consisted of chiropractic sacro occipital technique (SOT) and cranial treatment. Within the past year laboratory tests were instituted to monitor neurotransmitter balance of the HPA axis and used to help direct nutritional supplementation. The patient was seen once per week for chiropractic care and laboratory tests, while usually performed every 4 months, in this case was performed annually. This was due to the patient not performing the laboratory tests in a timely manner, believed due to her profile, which included inability to cognitively function in scheduling situations.

Results/Effects

Overall all of her symptoms improved which included headaches, which are less frequent, and less debilitating. The headaches went from being daily constant, and chronic to 2–3 times per week with significantly less intensity and debilitation, allowing her to function in her activities of daily living. Prior to care, she could not function when she had a headache. While she was making good progress with the chiropractic care during the 1st two-years, when nutritional supplementation based on laboratory analysis for neurotransmitter balance was instituted, headaches and function improved, including better sleep patterns and mental clarity.

Conclusions/Limitations

Treatment of brain trauma is a very individualized process and what may help one patient may not help another. It is unclear with case reports whether effective treatment for one patient can be generalized to the brain trauma population at large. However, it is worthy of consideration when a patient does not respond, or has an adverse reaction to medications and is non-responsive to traditional approaches, that a chiropractor trained in SOT and cranial treatments might be considered for collaborative care. Greater research is needed in interdisciplinary settings to determine how this subset of patients may be best served.

0079

Dynamic Postural Instability in OEF/OIF Veterans with Mild TBI and Disequilibrium

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Introduction/Rationale

Dizziness and imbalance are common symptoms in acute concussion and are also seen frequently in the post-concussive syndrome after both blunt and blast trauma. There are several forms of post-concussive dizziness, including positional vertigo, migraine-related dizziness, and subjective imbalance. The latter is the least understood and is often not easy to recognize clinically. The goal of this study is to quantify dynamic postural stability in veterans of Operation Enduring Freedom / Operation Iraqi Freedom (OEF/OIF), with a history of combat-related mild traumatic brain injury (mTBI), who report persistent disequilibrium.

Method/Approach

9 OEF/OIF veterans with mTBI and persistent disequilibrium and 10 subjects with no history of mTBI were studied. Subjects were perturbed abruptly by a rope attached to a waist-level belt and pulled by a computer-controlled linear actuator, in two directions (forward and to the side), and with eyes open and closed. We recorded body kinematics using an infrared motion tracking system with reflective markers on the head trunk and legs. The length of the two-dimensional (2D) sway path was calculated over the first three seconds after the onset of each perturbation.

Results/Effects

Sway paths (measured at the sacrum) were much longer for the mTBI group with disequilibrium (median 38.1 cm) than for the non-TBI group (median 16.9 cm). Using a repeated-measures ANOVA analysis, it was found that sway path lengths were significantly longer for mTBI vs non-mTBI ($p < 0.05$), for eyes closed vs. eyes open ($p < 0.03$), but not for the direction of the pull.

Conclusions/Limitations

Dynamic postural stability is impaired in OEF/OIF veterans with persistent disequilibrium following mTBI. Although these deficits may be relatively mild and are typically not apparent during routine clinical examination, they could have a critical impact on balance in unfamiliar and physically challenging environments, such as during combat.

0081

Posttraumatic Stress Disorder following an Offshore Explosion

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Introduction/Rationale

The purpose of this study was to explore the posttraumatic stress disorder (PTSD) symptomatology in individuals who experienced an explosion on an offshore rig. According to the Diagnostic and Statistical Manual-IV-TR for an individual to have PTSD they must have: (1) experienced or witnessed a traumatic event; and/or (2) experienced intense fear, or horror. If at least one of those criteria is met, they must also meet the following criteria: (1) intrusive recollection; (2) avoidance; (3) hyper-arousal. The study attempted to answer the question: What trauma-related symptoms were present following the explosion that were not present prior to the explosion?

Method/Approach

This case study included four participants between the ages of 22 and 29 ($M = 26$). Each of the participants received a complete neuropsychological evaluation by a psychologist. Among the four participants, one participant had obtained a pre-morbid head injury and a medical diagnosis. No participants had a remarkable history.

Results/Effects

The results showed that all of the participants had PTSD and three of them also had a post-concussion. The symptoms they reported were intrusive thoughts, flashbacks, avoidance behaviors, nightmares, hyper-vigilance, anxiety, and fear. Among the four participants, two of them also reported jumpiness, fear of being lost, and guilt. Each of them provided an initial trauma narrative that contained similar descriptions of events with vivid recollections.

Conclusions/Limitations

Based on the results of the study, individuals exposed to an explosion experience many trauma-related symptoms that meet criteria for PTSD. Although it cannot be concluded that all individuals exposed to this environmental disasters were negatively affected, it can be concluded that these individuals suffered similar trauma-related symptoms and provided similar, vivid trauma narratives.

0082

Successful Scholastic Reintegration: Academic, Social and Behavioural Success for Students with ABI

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Introduction/Rationale

Students spend approximately 30% of their waking hours in school, providing both a natural and appropriate environment for psychosocial rehabilitation. This is especially important given that student's socio-emotional, behavioural, and scholastic outcomes after sustaining an acquired brain injury (ABI) are incredibly variable and independent of injury severity. Within the province of Ontario, ABI is not a recognized exceptionality within the school system, which impacts the student's ability to access the multitude of resources often required post-ABI. This province and Centre-wide research project serves to examine student-, parental-, teacher-, and school policy-based variables that influence students' successful reintegration within the school system.

Method/Approach

Students between the ages of 6 – 18 years, who are 1 – 5 years post-injury, were identified by health care providers and approached to consider participation in the study along with their respective parents. Their teachers and principals were approached with permission of the students and their respective school boards. Participants completed status-appropriate standardized and non-standardized measures (i.e., students were assessed with psycho-educational and neuropsychological tests and self-report measures; parents, teachers and principals completed questionnaires related to history, status, ABI knowledge, school policy, and the student). Regression analyses were conducted to identify variables that best predicted successful reintegration.